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Novel two-step hierarchical screening of mutant pools reveals mutants under selection in chicks

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Abstract

© 2016, American Society for Microbiology. All Rights Reserved.Contaminated chicken/egg products are major sources of human salmonellosis, yet the strategies used by Salmonella to colonize chickens are poorly understood. We applied a novel two-step hierarchical procedure to identify new genes important for colonization and persistence of Salmonella enterica serotype Typhimurium in chickens. A library of 182 S. Typhimurium mutants each containing a targeted deletion of a group of contiguous genes (for a total of 2,069 genes deleted) was used to identify regions under selection at 1, 3, and 9 days postinfection in chicks. Mutants in 11 regions were under selection at all assayed times (colonization mutants), and mutants in 15 regions were under selection only at day 9 (persistence mutants). We assembled a pool of 92 mutants, each deleted for a single gene, representing nearly all genes in nine regions under selection. Twelve single gene deletion mutants were under selection in this assay, and we confirmed 6 of 9 of these candidate mutants via competitive infections and complementation analysis in chicks. STM0580, STM1295, STM1297, STM3612, STM3615, and STM3734 are needed for Salmonella to colonize and persist in chicks and were not previously associated with this ability. One of these key genes, STM1297 (selD), is required for anaerobic growth and supports the ability to utilize formate under these conditions, suggesting that metabolism of formate is important during infection. We report a hierarchical screening strategy to interrogate large portions of the genome during infection of animals using pools of mutants of low complexity. Using this strategy, we identified six genes not previously known to be needed during infection in chicks, and one of these (STM1297) suggests an important role for formate metabolism during infection.

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